REMARKS

Claims 1, 28-31 and 33-47 are pending. No new matter has been added by way of the present submission. For instance, claim 1 has been amended to include subject matter taken from claim 32, now cancelled, as well as the present specification at page 9, lines 11-13, and page 15, line 14 to page 16, line 2. Also, claim 1 has been amended so as to correctly recite a microroughness comprising pores having a pore diameter of ≤ 1 μm and a pore depth of ≤ 500 nm as supported by the application as filed. Claim 33 has been amended to depend upon claim 1. Lastly, claim 38 has been clarified as supported by at least the above noted disclosures of the present specification. Thus, no new matter has been added.

In view of the following remarks, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

Provisional Obviousness-type Double Patenting

The Examiner has provisionally rejected claims 1 and 28-47 under the judicially created doctrine of obviousness-type double patenting as being obvious over certain claims of Application No. 10/519,495. Applicants traverse and point out that Application No. 10/519,495 is abandoned, thus, this issue is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issue under 35 U.S.C. § 103(a)

Claims 1 and 28-47 have been rejected under 35 U.S.C. § 103(a) as being obvious over Ellingsen et al., WO 95/17217 optionally in view of Steinemann et al., USP 5,456,723 and Haruyuki et al., JP 3146679. Applicants respectfully traverse this rejection.

The Present Invention and its Advantages

Independent claim 1 relates to a method for treating an implant surface intended for implantation into bone tissue, said method comprising:

providing fluorine and/or fluoride on at least a part of the implant surface, and

providing a microroughness comprising pores having a pore diameter of ≤ 1 μm and a pore depth of ≤ 500 nm, wherein the implant surface is a metallic implant surface, by treating the metallic implant surface with an aqueous solution of hydrofluoric acid, resulting in an etching process, wherein the concentration of the hydrofluoric acid is less than 0.5 M, and wherein the metallic implant surface is treated for an etching period of up to 180 seconds at room temperature, said etching period being measured from the formation of the first bubble of H_2 (g) at the implant surface.

Independent claim 38 is directed to an implant for implantation into bone tissue having an implant surface, wherein

the implant surface is a metallic implant surface,

there is an oxide layer on at least part of the implant surface,

said oxide layer having fluorine and/or fluoride incorporated therein, and

at least a part of the implant surface comprises a microroughness which comprise pores having a diameter of < 1 μm and a pore depth of < 500 nm, wherein the microroughness comprises peaks having a peak width, at half the pore depth, of from 15 to 150% of the pore diameter.

According to the present invention, a surface roughness comprising pores and peaks having a diameter of ≤ 1 μm, and a pore depth of ≤ 500 nm has been shown to give surprisingly good biocompatibility results. For instance, it has been shown that surprisingly good biocompatibility results are obtained with an implant having the above mentioned microroughness parameters. Both an improved rate of attachment and a stronger bond between the implant surface and the bone tissue are obtained. Thus, the fine microroughness improves the osseointegration process. Such surface roughness is achieved according to the present method wherein the metallic implant surface should be treated with an aqueous solution of HF under specific etching conditions.

Distinctions Between the Present Invention and the Cited Art

1. Claim 1 (method) and Claims dependent thereon are non-obvious

The method as defined in claim 1 presently on file includes treatment of the implant with hydrofluoric acid such that etching occurs. The etching process provides a desired microroughness on the implant surface. The etching period, which is measured from the formation of the first bubble of H_2 (g) at the implant surface, may take place for up to 180 seconds at room temperature.

Prior to commencement of etching, a natural oxide layer, which is conventionally

present, is removed by the acid and when the acid contacts the metallic surface, the etching process starts. A new oxide layer with fluorine and/or fluoride incorporated therein and distributed throughout the oxide layer is then formed. As will be seen below, the cited art fails to render such subject matter obviousness. Moreover, even if hypothetically obvious, the present implant unexpectedly provides improved osseointegration and resistance to bone in-growth. Such unexpected results are quite superior to the prior art and thus rebut any hypothetical *prima facie* case of obviousness.

There exists no *prima facie* case of obviousness

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab,* 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). *See also In re Lee,* 277 F.3d 1338, 1342-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (discussing the importance of relying on objective evidence and making specific factual findings with respect to the motivation to combine references); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

The Supreme Court of the United States has held that the teaching, suggestion, motivation test is a valid test for obviousness, but one which cannot be too rigidly applied. See

KSR Int'l Co. v Teleflex Inc., 127 S.Ct. 1727, 82 USPQ2d 1385 (U.S. 2007). The Supreme Court in *KSR Int'l Co. v. Teleflex, Inc.*, *ibid.*, reaffirmed the *Graham* factors in the determination of obviousness under 35 U.S.C. § 103(a). The four factual inquiries under *Graham* are:

(a) determining the scope and contents of the prior art;

(b) ascertaining the differences between the prior art and the claims in issue;

(c) resolving the level of ordinary skill in the pertinent art; and

(d) evaluating evidence of secondary consideration.

Graham v. John Deere, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (U.S. 1966).

The Court in *KSR Int'l Co. v. Teleflex, Inc., supra.,* did not totally reject the use of "teaching, suggestion, or motivation" as a factor in the obviousness analysis. Rather, the Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a).

Even so, the Court in *KSR Int'l Co. v. Teleflex, Inc., ibid.,* rejected a rigid application of the "teaching, suggestion, or motivation" (TSM) test, which required a showing of some teaching, suggestion, or motivation in the prior art that would lead one of ordinary skill in the art to combine the prior art elements in the manner claimed in the application or patent before holding the claimed subject matter to be obvious.

Further, the Examiner bears the initial burden of presenting a *prima facie* case of obviousness. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). "[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the

legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336, quoted with approval in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007).

The primary reference applied by the Examiner is Ellingsen. Applicants will first explain why Ellingsen fails to suggest or disclose the presently claimed subject matter. Then, Applicants will explain why the additional secondary references cannot make up for the failings of Ellingsen. The result of these combined failings is that even if the art is taken as a whole, the present invention is nonetheless non-obvious.

ELLINGSEN

Ellingsen disclose a method for treating an implant surface with an aqueous solution of hydrofluoric acid. As the Examiner admits, Ellingsen fails to disclose the formation of micropores, but rather, Ellingsen indicates that there is most preferably substantially no etching of the implant surface. In other words, the treatment may result in removal of the oxide layer, but does not result in any etching. Thus, an implant obtained by the method of Ellingsen will not have the same surface characteristics as the inventive implant.

It is clear from the teaching of Ellingsen that the improved biocompatibility was attributed to fluoride being retained on the surface of the implant. Thus, it can be concluded that Ellingsen did not recognize that a further improved biocompatibility could be obtained by also providing a microroughness on the implant surface. On the contrary, Ellingsen stipulate that no significant etching shall occur; the implant of Ellingsen is unaffected by the proposed HF treatment, and this is also supported in Figure 2 and discussed on page 15, lines 4-8 of Ellingsen.

At this point the Examiner's rejection must fail. Specifically, for the Examiner's rejection to succeed, one of skill in the art must modify Ellingsen in a manner directly contrary to the teachings of Ellingsen. Specifically, the desire of Ellingsen to have substantially no etching of the implant surface, must be replaced with the desire to provide etching, and specifically the etchings required by the present claims. However, such a modification is improper in presenting a valid *prima facie* case of obviousness. Indeed, one of skill in the art looking to solve the problems disclosed by the prior art references would not modify Ellingsen as suggested by the Examiner since this would destroy the teachings of Ellingsen. Where the Examiner's proposed modification would render the prior art version unsatisfactory for its intended purpose, the proposed combination is improper. *In re Gordon*, 733 F.2d 980, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984); *see also Ex parte Rosenfeld*, 130 USPQ 113 (POBA 1961).

Regardless, the Examiner has made a remark that the inventive examples (page 8, paragraphs [0107] to [0116]) do not disclose how long the implants are exposed to the HF acid solution before the etching period begins. In this regard, Applicants point out that the treatment according to the present invention is based on the surprising finding that implants having excellent osseointegration properties can be obtained by subjecting them to a certain etching period. This etching period is defined as the process taking place during the treatment period during which H_2 (g) is generated at the implant surface. The etching period is measured from the formation of the first bubble of H_2 (g) at the implant surface.

Before etching starts, the natural oxide layer is removed by the acid, and when the acid gets in contact with the implant surface, the etching process starts. The length of the time period preceding the etching process depends, e.g., on the thickness of the natural oxide layer, and also

on the geometry of the implant.

From the teachings of Ellingsen, a man of ordinary skill in the art is taught that an improved biocompatibility can be obtained by treating a metallic implant surface with a solution of HF acid during a certain time period. However, at the same time, Ellingsen very clearly states that etching should preferably not occur. Thus, in practicing the teaching of Ellingsen, a man of ordinary skill in the art would immediately interrupt the HF treatment at the point where etching begins. This is a fundamental difference in view of the present invention, where the time period of HF treatment is measured from the point where the etching begins.

In view of the above, it can be concluded that the time period preceding the etching period in the inventive examples is not relevant. What is relevant in the comparison between the inventive implants and the prior art implants is that the treatment of the prior art implants (treated in accordance with the process disclosed by Ellingsen) did not result in any etching. With reference to the specification on page 6, paragraph [0105], it can be seen that the treatment of the prior art implants indeed were not subjected to any etching: "No H_2 (g) was formed during this treatment period, thus no etching occurred."

In summary, there is neither hint nor indication in Ellingsen that the creation of surface irregularities could be favorable to improved osseointegration. Instead, the improved biocompatibility is thought to be due to fluoride being retained on the implant surface. Therefore, one of ordinary skill in the art would have no incitement whatsoever to modify the fundamentals of Ellingsen, saying that no significant etching should occur.

Thus, it would not have been obvious to modify the method of Ellingsen in the direction of the present invention. Neither would it be obvious to arrive at the invention when applying the

teaching of Ellingsen in view of Steinemann or Haruyuki, as discussed below.

STEINEMANN

Steinemann discloses an implant intended for use in a bone, where the surface of the implant has a micro-roughness with a pore size in the order of magnitude of 2 μm and less. The micro-roughness is superimposed on a macro-roughness with pore sizes of the surface of more than 10 μm. The method for manufacturing the implant of Steinemann comprises

(i) blasting the surface of the implant with a blasting medium for the production of a macro-roughness and

(ii) allowing a reducing acid, e.g. HF, to act on the implant for the production of a micro-roughness.

Although Steinemann teach that the microroughness can be obtained with treatment with hydrofluoric acid, they are completely silent as to what specific conditions are required for the surface treatment, such as HF concentration, immersion time and temperature. Steinemann shows no example of treatment with HF. The only example in accordance with the subject-matter claimed in Steinemann (Example VI) relates to dipping in a bath of $HCl + H_2SO_4$.

With regard to the specific conditions used for example VI, it can be seen (col. 5, lines 25-26) that the acids are used in concentrations of 30 % (HCl) and 60 % (H_2SO_4). Furthermore, the acid treatment is performed at boiling temperature for 1 minute (col. 5, line 26). Steinemann also explicitly states that the reducing acid is preferably made to exert its action in its boiling state (col. 3, line 15).

Thus, Steinemann give no guidance whatsoever in the direction of the present invention.

On the contrary, Steinemann indicate that the concentration of acids used needs to be very high (30 %, 60 %), and furthermore that the acid treatment shall be made in a boiling state. This is in great contrast to the present invention, according to which the acid treatment is performed at room temperature and the concentration of HF is less than 0.5 M. Applying the teachings of Ellingsen in view of Steinemann would certainly not lead to the surface irregularities according to the present invention.

HARUYUKI

Haruyuki relate to a two-step treatment of an implant surface to provide fine irregularities with an average pore size of 1-10 μm and an average depth of 0.5-5 μm on the surface. The treatment involves:

(i) immersion from 30 seconds to 3 minutes in an aqueous solution of 1-6 % (w/w) hydrofluoric acid (HF), followed by

(ii) immersion from 10 to 60 seconds in a mixed solution of 1-6 % (w/w) hydrofluoric acid (HF) and 1-10 % (w/w) hydrogen peroxide (H_2O_2).

The purpose of the first step is to remove the oxide film and other contaminants from the surface and provide fine irregularities with an average pore size of 1-10 μm and an average depth of 0.5-5 μm on the surface. The purpose of the second step is to smooth the sharp edges and thorns formed during the first treatment step. This treatment is said to improve the adhesion strength between implant and bone.

According to Haruyuki, a HF concentration below 1 % in the first step is not considered applicable since the pore size of the surface irregularities will then not reach 1 μm (see page 4,

col. 1, lines 12-13). A pore size below 1 μm is considered as not desirable since the adhesive force to the cells is then believed to be reduced (see page 4, col. 1, lines 14-16). Accordingly, from the teachings of Haruyuki, the skilled man would learn that to improve biocompatibility, a HF concentration over 1 % should be used. Thus, Haruyuki teaches away from the present invention, which stipulates a HF concentration of less than 0.5 M (corresponding to a HF concentration of less than 0.8 % w/w).

Furthermore, in the second treatment step of the process according to Haruyuki hydrofluoric acid and hydrogen peroxide are used. The use of hydrofluoric acid alone is neither disclosed nor suggested in Haruyuki.

Applying the teachings of Ellingsen in view of Haruyuki would not be sensible in the first place, because Ellingsen teaches that no significant etching should occur. In the unlikely event that the teachings of Ellingsen should nevertheless be applied in view of Haruyuki, the only reasonable conclusion would be that HF treatment of Ellingsen should be replaced by a two step treatment, and furthermore that a HF concentration over 1 % should be used. This treatment would certainly not lead to the surface irregularities according to the present invention.

2. Claim 38 (implant) and Claims dependent thereon are non-obvious

The implant according to claim 38 comprises a microroughness comprising pores having a diameter of ≤ 1 μm and a pore depth of ≤ 500 nm, and peaks having a peak width, at half the pore depth, of from 15 to 150 % of the pore diameter. Furthermore, the implant according to claim 38 contains an oxide layer incorporating fluorine and/or fluoride ions therein.

This specific surface morphology gives a very resistant bone in-growth: newly formed

bone, which grows into the surface irregularities of the implant surface, does not easily fracture from the old bone. In addition, the peaks of the implant surface do not easily fracture from the implant. (See paragraph [0065] of the present application).

A titanium oxide with incorporated fluorine and/or fluoride has a disturbed oxide structure as compared to the ordinary pure titanium oxide structure. It has surprisingly been found that this disturbed oxide gives a more reactive oxide layer, which means that the oxide in vivo to a higher degree interacts with molecules, such as phosphate ions, and also grows at a higher rate, which means that an improved biocompatibility is obtained. (See paragraph [0076] of the present application).

Ellingsen clearly teach that there is most preferably substantially no etching of the implant surface (see p. 8, lines 1-3). Accordingly, Ellingsen fail to disclose <u>any</u> microroughness parameters. Ellingsen attribute the improved biocompatibility at least in part to fluoride being retained <u>on the surface</u> of the implant. Nowhere in Ellingsen is it taught or suggested that providing a microroughness in accordance with the present invention would improve osseointegration. Neither do Ellingsen recognize that the incorporation of fluorine and/or fluoride ions <u>in the oxide layer</u> would further enhance the biological acceptance of the implant.

The superiority of the implants according to the invention is shown by the examples provided in the application; with reference to Table 1 on page 7, it can be seen that the implants according to the invention gave an improved bone attachment as compared to the implants according to Ellingsen.

Steinemann and Haruyuki do not disclose the microroughness parameters suggested according to the present invention, i.e. a microroughness comprising pores having a diameter of

$\leq 1\ \mu m$ and a pore depth of ≤ 500 nm, and peaks having a peak width, at half the pore depth, of from 15 to 150 % of the pore diameter. In addition, neither Steinemann nor Haruyuki teach or suggest that incorporation of fluorine and/or fluoride in the oxide layer would be favourable for obtaining a better attachment of the implant. Thus, a skilled man would have no incentive to modify the implant surface accordingly.

Applicants respectfully disagree that it would be obvious from prior art (Steinemann and Haruyuki) that small amounts of acid etching improve osseointegration of an implant. As was evidenced above, the prior art suggests completely different etching methods which would require significant adaptations to approach the findings of the present invention. Applying the process conditions suggested by Steinemann and Haruyuki in view of Ellingsen would certainly not lead to the present invention.

In the research work leading to the present invention, it was surprisingly found that an implant surface having superior characteristics can be obtained by carefully selecting the process conditions under which the surface is prepared. In particular, the present invention provides for a surface morphology giving an improved rate of attachment, and a stronger bond between the implant surface and the bone tissue (see page 2, paragraph [0027]). In order to achieve this optimal surface morphology, the process conditions must be combined in a specific and predetermined manner. Minor adjustment of one process parameter may have a major impact on the final result.

In view of the above, Applicants respectfully submit that there exists no prima facie case of obviousness. Alternatively, any hypothetical prima facie case of obviousness is rendered moot by the unexpectedly superior results of the present invention. The Examiner is therefore

requested to withdraw this rejection and allow the currently pending claims.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie (Reg. No. 42,874) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By____________________

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